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(54) Improved liquid
chromatography apparatus

(57) The apparatus includes a light source for directing a light beam through measurement zone 54 to a detector. Movement of the beam in a measurement direction with respect

to the detector gives an indication of the measurement made in the zone. Sample fluid, the refractivity of which is to be measured, is delivered to the zone along inlet tube 20 which is in heat-exchanging relationship with outlet tube 22 for carrying the sample from the zone.

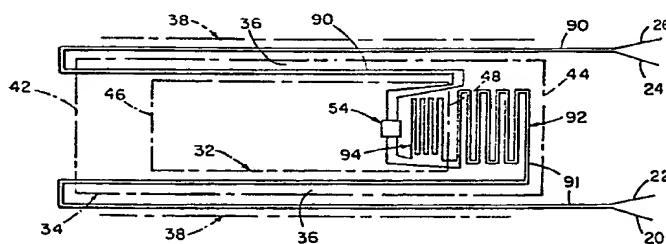


FIG 6

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FIG. 2

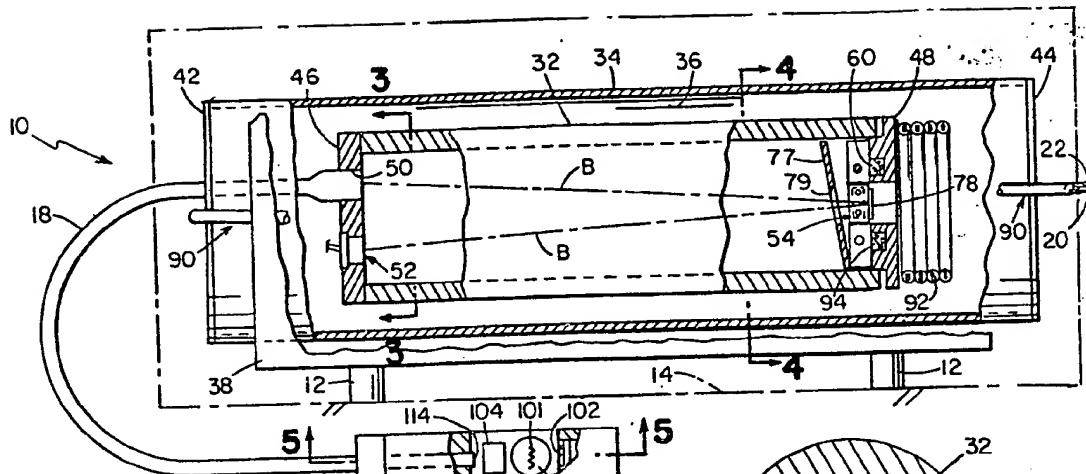


FIG. 5

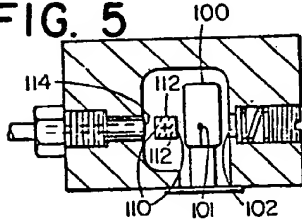


FIG. 3

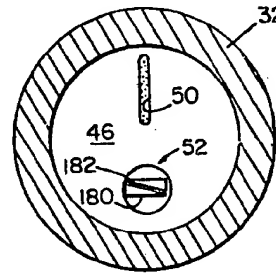


FIG. 1

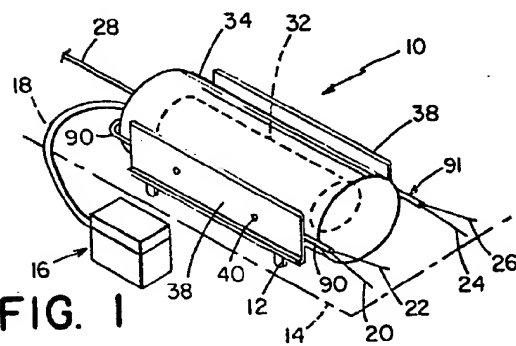


FIG. 4

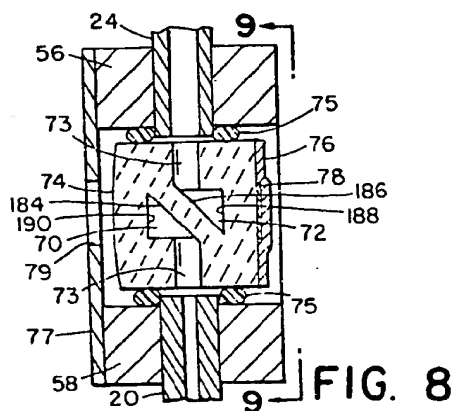
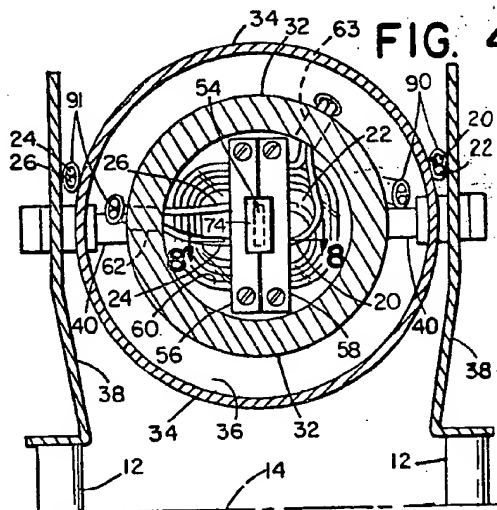


FIG. 8

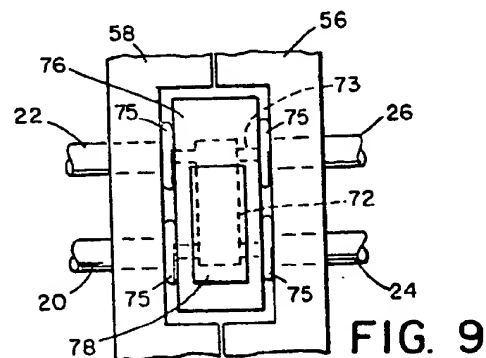


FIG. 9

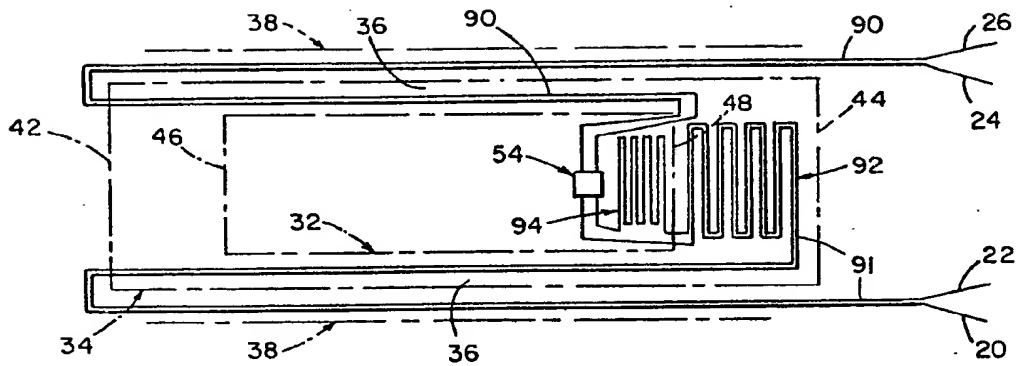


FIG 6

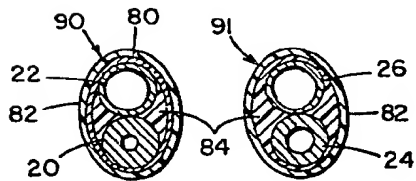


FIG 7a

FIG 7b

FIG 10a

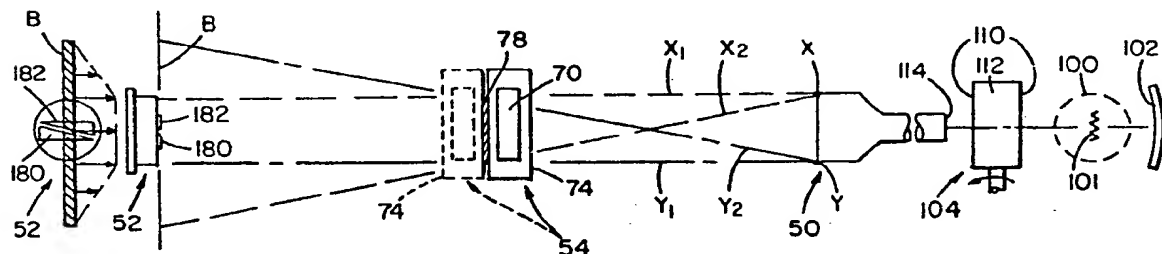
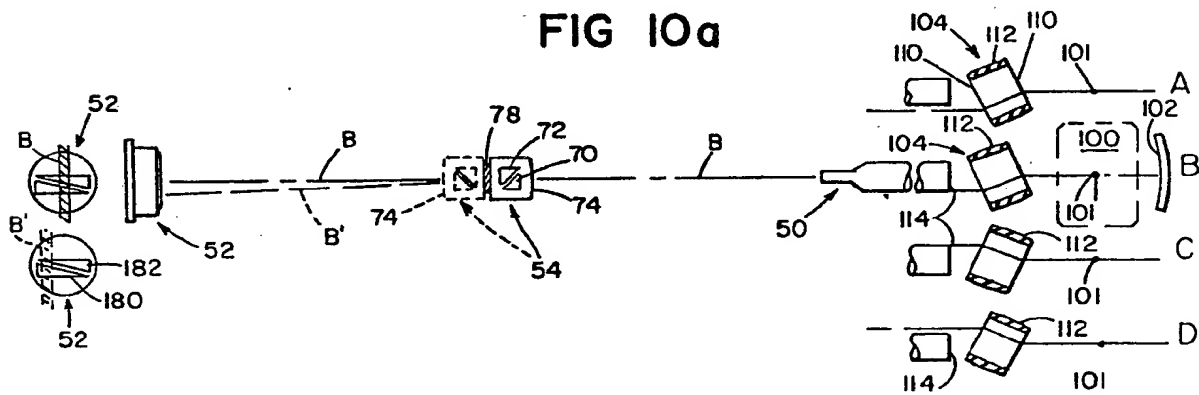
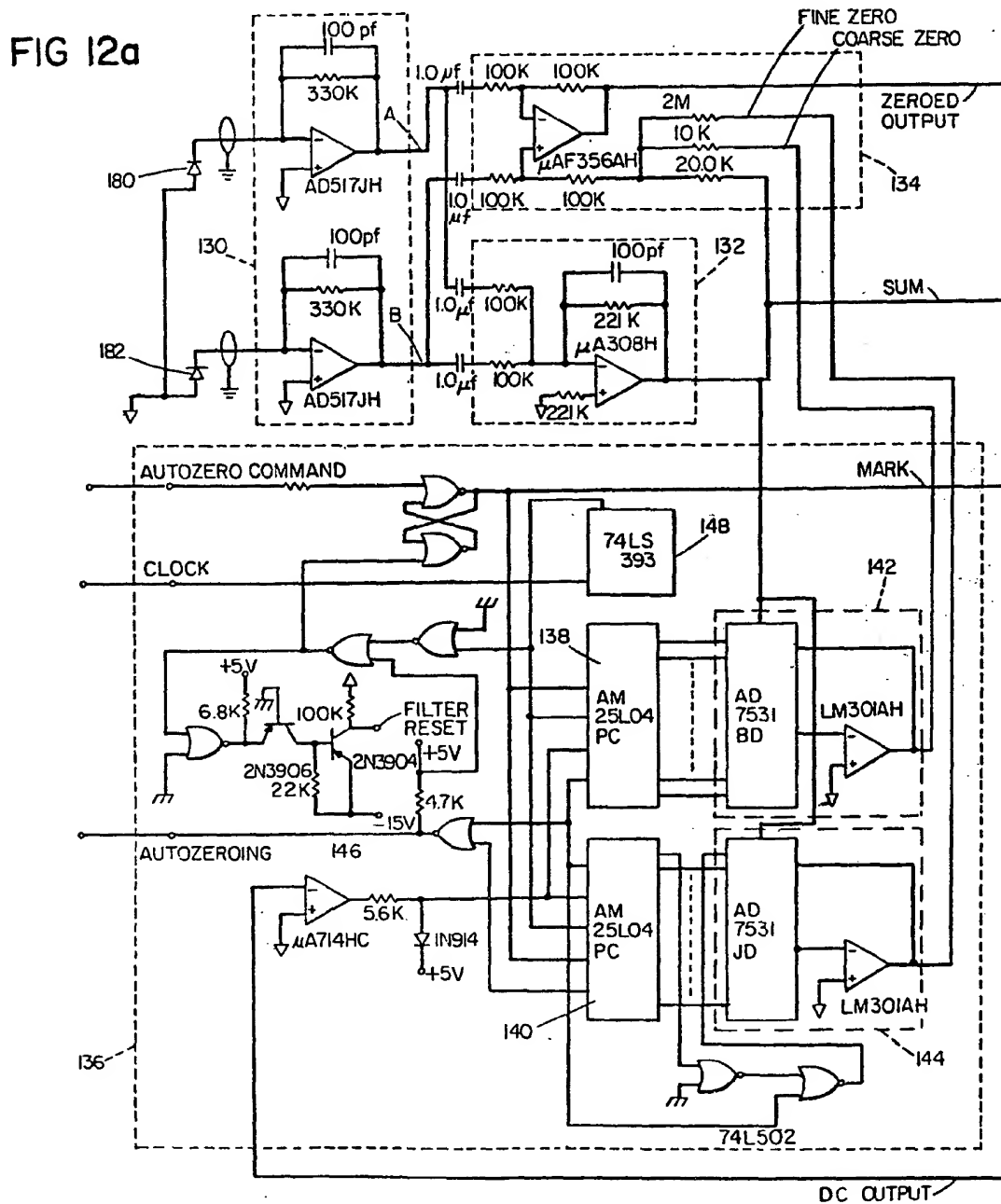
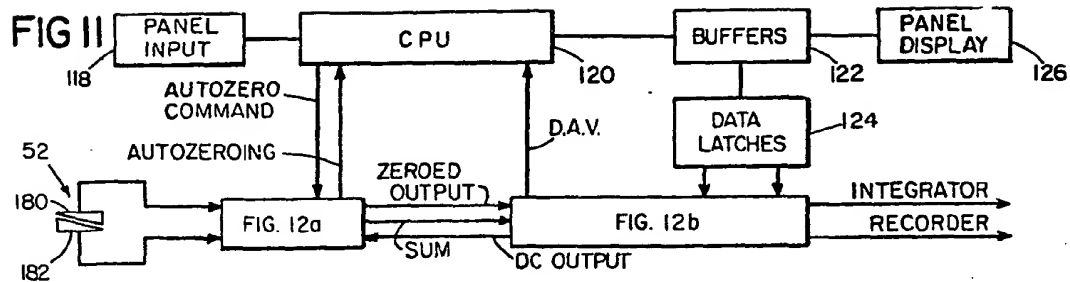
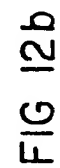


FIG 10b





SPECIFICATION

Improved liquid chromatography

This invention relates to light-beam deflection instruments, such as refractometers. In such instruments, a light source typically directs a beam through a test cell to a detector (e.g., a photocell). A change in some physical quantity (e.g., refractivity) causes the light beam to move with respect to the detector.

- 10 This invention relates to devices which depend upon accurate measurement of changes in the refractivity of a flowing fluid, e.g., in liquid chromatography. Because temperature affects refractivity, the temperature of the flowing liquid must be carefully controlled. Typically in refractive index detectors used in liquid chromatography the refractivities of sample and reference streams are compared at a cell. One technique for equalizing temperature in the sample and reference streams in the cell has been to supply the fluid to the cell after having passed through sample and reference inlet tubes in heat-exchanging relationship with each other and with a large metal block. Ideally, both streams are at equal temperatures before entering the cell.

- 25 According to the invention there is provided apparatus for measuring changes in the refractivity of a fluid flowing through a temperature-controlled cell, wherein an inlet tube carrying sample fluid to said cell and an outlet tube for carrying sample fluid from said cell are mounted in a heat-exchanging relationship with each other.

- 35 With the invention better control over temperature can be achieved as a result of the heat-exchanging relationship between the sample inlet (to the cell) and sample outlet (from the cell) streams. The required hardware is simpler and inexpensive. Excellent temperature equalization of sample and reference fluids, and very fast warm up and cool down of the device, are made possible.

- 45 We have discovered that increased light throughout can be achieved in the cell of a refractometer by placing an integral reflective layer on or within the cell, to reflect the light beam back through the cell. Parallax between the flow cell chambers and the reflective surface is reduced. Fewer surfaces are exposed to the ambient, thereby reducing losses due to dust buildup and surface reflection. Manufacturing is simplified as fewer parts are required.

- 55 We have also discovered an improved zeroing technique which is relatively insensitive to changes in light intensity, and which, in preferred embodiments, eliminates optical zeroing. In general, we include in the system output a main term dependent on the difference between the two optical measurements and an offset term dependent on at least one such measurement. Any change in light intensity will substantially equally affect the main and offset terms, so as to maintain zeroing accuracy.

We have discovered that increased light

- 65 throughout can be achieved in the cell of a refractometer by incorporating an integral curved surface with the cell, to act as a lens for focusing the light beam. Parallax between the flow cell chamber and the lensing surface is reduced. Fewer surfaces are exposed to the ambient; thereby reducing losses from dust build-up and surface reflection. Manufacturing is simplified as fewer parts are required. Embodiments of the invention may incorporate an opaque mask within or on the flow cell.

- 75 Embodiments of the invention may comprise circuitry for analog-to-digital and digital-to-analog conversion and similar operations.

- 80 A digital circuit is usually faster operating than an analog circuit, and thus the time required to complete each sequence of steps is largely controlled by the response time of the analog circuit. For example, if the analog circuit includes a filter for smoothing out ripple and noise, it may require a few seconds for the output of the analog circuit to reach a new value. When these few seconds are multiplied by the number of times the sequence is repeated the lost waiting time can be considerable. We have discovered that the time lost waiting for the analog circuit to respond can be shortened by dissipating (e.g., with a switch connected in parallel) the charge-storage device (e.g., capacitor) in the analog circuit. After dissipation, the analog circuit and charge-storage device are allowed to respond normally.

- 90 The structure and operation of a preferred embodiment of the invention will now be described, after first briefly describing the drawings, in which:

- 100 Fig. 1 is a perspective view of said embodiment,

Fig. 2 is a partially cross-sectional view of said embodiment,

- 105 Fig. 3 is a cross-sectional view at 3—3 of Fig. 2, showing the photocell end of the optical bench,

- Fig. 4 is a cross-sectional view at 4—4 of Fig. 2, showing the flow cell end of the bench and the outer insulating cylinder and shields, with internal heat shield/light baffle 77 removed,

- 110 Fig. 5 is a cross-sectional view at 5—5 of Fig. 2, showing the light source,

Fig. 6 is a schematic of the heat exchanger plumbing,

- 115 Fig. 7a and 7b are cross-sectional views through the sample and reference heat exchangers, respectively,

Fig. 8 is a cross-sectional view at 8—8 of Fig. 4, showing construction of the flow cell,

- 120 Fig. 9 is an elevation view of the back surface of the flow cell at 9—9 of Fig. 8,

Figs. 10a and 10b are diagrammatic views of the optical path through said embodiment,

Fig. 11 is a block diagram of the electronics that process the outputs of the photocells, and

- 125 Figs. 12a and 12b are schematics of the electronic circuits that null the photocell output and process the nulled output for display and integration.

Turning to Fig. 1, an optical bench 20 is

supported inside an oven on four insulating posts 12 attached to a floor 14 of the oven. A light source 16 for the bench is positioned below the bench and outside of the oven. A fibre-optic cable 18 carries light from the source 16 to the bench. Sample liquid from the outlet of a chromatographic column (not shown) positioned inside the oven flows into the optical bench through an inlet tube 20 (0.009 inch ID), and out through an outlet tube 22 (0.040 inch ID). A small diameter sample inlet tube is used to minimize band spreading in the chromatogram. Similarly, reference liquid flows into and out of the bench through an inlet tube 24 (0.020 inch ID) and an outlet tube 26 (0.040 inch ID). All four tubes are stainless steel and have 1/16 inch outside diameters. The outlet tubes have larger internal diameters than those of the inlets to lower backpressure and its effect on refractivity. The outlet tubes 22, 26 are connected together downstream of the optical bench to equalize sample and reference pressures at the flow cell. Electrical wires 28 from photocells 52 (Fig. 2) lead from the bench to processing circuits shown in Figs. 11, 12a, and 12b.

Turning to Figs. 2, 3 and 4, the optical bench 10 consists of an inner cylinder 32, through which a light beam B is passed, and a concentric outer cylinder 34, which provides an insulating air gap 36. Two flat shields 38 (Fig. 1) retard radiation of heat to and from the bench, and act as legs (Fig. 4) to support the cylinders, via four bolts 40, on posts 12. End caps 42, 44 close each end of the outer cylinder 34, and end caps 46, 48 each end of the inner cylinder 32. The end cap 46 supports an elongated outlet 50 (0.050 inches wide by 0.35 inches high) of the fibre-optic cable 18 and photocell 52. The end cap 48 supports the flow cell 54 via cell bridges 56, 58, which are attached to the cap and each other by screws and epoxy. The sample inlet and outlet tubes 20, 22 terminate at the bridge 58; the reference tubes 24, 26 terminate at the bridge 56. A recess 60 in the end cap 48 behind the bridges contains about four coils of the sample inlet tube 20. Notches 62, 63 in the inner cylinder 34 provide entryways for the tubes. The end caps, cylinders, and shields are all made from aluminium, to speed warm up of the bench while also insulating the bench by virtue of the air gap 36 between the cylinders.

Turning to Figs. 8 and 9, the flow cell 54 has two hollow chambers 70, 72, for the sample and reference liquids, respectively. Each chamber has a triangular (about 45 x 45 x 90 degrees, 0.062 inches on each short side) cross section (Fig. 8), and is connected to its respective inlet and outlet tubes by internal passages 73. The height (or vertical dimension in Fig. 9) of the chambers is about 0.50 inches. The flow cell is manufactured by fusing together, without adhesive, pieces of borosilicate glass. Teflon (trade mark) seals 75, compressed against the cell by the bridges, provide a seal between the sample and reference tubes and the internal passages 73 of the cell. The front surface 74 of the flow cell is ground to provide an

integral lens that has curvature in horizontal but not vertical planes. The back surface of the cell has a reflective surface coating 78 of gold to provide a mirror to reflect light back through the chamber 70, 72 to the photocell 52. The focal line of the lens is positioned at the photocell 52, and the spacing between the mirror 78 and the photocell 52 is about 6.0 inches. As shown in Fig. 9, the mirror coating 78 is limited to approximately the area directly behind the chamber 72, thereby to limit reflection principally to light passing through the triangular chambers. Other light is absorbed by a black epoxy coating 76 applied over and around the mirror coating. The mirror coating is slightly larger than the chambers to accommodate variations in the internal size of the chambers 70, 72. The coating stops short of the top of the chambers 70, 72 (Fig. 9) so as not to reflect light passing through the top of the chambers, where bubbles might form.

To reduce radiant and convective heat transfer to the flow cell from within the optical bench, a blackened disk 77 with a rectangular light-beam aperture 79 (just large enough to expose the flow cell) is positioned ahead of the flow cell. This disk also serves as a light baffle, and is tilted down 10° (Fig. 2).

Sample and reference liquid are brought into the flow cell through sample and reference counterflow heat exchangers 90, 91 (Figs. 1, 6, and 7), each of which are formed by bonding corresponding inlet and outlet tubes together inside a tubular jacket. Each bonded pair is then routed along a multi-zone path beginning outside the bench and ending at the flow cell. As shown in Fig. 7, the sample heat exchanger 90 is constructed by placing the tubes 20, 22 inside a tubular copper braid 80, heat shrinking a polyethylene tube 82 over the outside of the copper braid, and filling the interstices between the braid and the inlet and outlet tubes with a low-viscosity, moderately-heat-conductive epoxy 84 such as Stycast (trade mark) 3051. Reference tubes 24, 26 are bonded without a copper braid by inserting the tubes inside a Teflon tube and filling the tube with the same low-viscosity epoxy as used for the sample tubes. The braid is omitted because less efficient heat transfer is needed for the reference, as it does not flow during measurement, but only during flushing between measurements.

Turning to Fig. 6, the multi-zone path followed by the heat exchangers is shown diagrammatically. The first zone for both sample and reference heat exchangers begins outside the optical bench and extends along the outside length of the bench between the outer cylinder 34 and the shields 38 (total zone length about 8 inches). The sample heat exchanger 90 is positioned on the side of the bench closer to the centre of the oven, where temperatures are better controlled. At the end cap 42, both heat exchangers turn 180° and enter the gap 36 between the cylinders 32, 34, through a slot (not

shown) in the end cap. The second zone for both sample and reference extends along the gap 36 (total length about 7 inches). The reference heat exchanger goes directly from the gap 36 into the cylinder 32 through the notch 62 in the end of the cylinder. Inside the cylinder 32, the reference inlet and outlet tubes are brought directly to the flow cell 54 via the bridge 56.

The sample heat exchanger 90 continues into a third zone beyond the end cap, where it is bent into a coil 92, consisting of four turns (total coil length about 24 inches) positioned in the space behind the end cap 48. The last turn is adjacent to the back of the end cap. From the coil the sample heat exchanger enters the cylinder 32 through the notch 63. Inside the cylinder, the sample outlet tube 22 is connected directly to the flow cell. The sample inlet tube 20 is wound in another coil 94 (total length about 12 inches) before entering the flow cell. The coil 94 is positioned in the recess 60, and potted with a heat-conductive epoxy to provide good conductivity with the end cap and cell bridges.

Turning to Figs. 2 and 5, the light source 16 includes an incandescent bulb 100 (Phillips 6336, H3 base, 6 V, 55W, operated at 4.8 V) with vertically-extending filament 101, a concave light-focusing mirror 102 (gold-coated glass), and a rotating prism 104. The prism is rotated at about 50 to 60 rpm along an axis parallel to the filament axis by a shaded-pole AC motor 106. The motor also drives a fan 108 which supplies cooling air to the bulb. The prism 104 is about 0.37 inches high, is made of glass, and has a rectangular cross section. Two opposite surfaces 110 of the prism are clear and about 0.3 inches wide. The other two surfaces 112 are opaqued with a white opaque silicone rubber, and are about 0.25 inches wide. A fibre-optic inlet 114 is round (about 0.150 inches in diameter) and is positioned opposite the prism from the bulb. The mirror 102 is positioned so as to focus an image of the filament 101 on the face of the inlet 114. The bulb 100 has a peak output in the near infra-red spectrum at a wavelength of about 1000 nanometers.

The fibre-optic cable 18 is broken internally into sub-bundles and the sub-bundles are intentionally disordered at one end to randomize the light path between the inlet 114 and the outlet 50.

The photocell 52 has two adjacent triangular dual photovoltaic cells 180, 182 (gold-bonded silicon) arranged so that their long dimensions extend horizontally, which is the direction of movement of the light beam. Each triangle is about 0.150 inches long and 0.05 inches high. The spacing between the triangles is about 0.008 to 0.010 inches. The shunt impedance at operating temperature (about 150°C) is maximized, as is the sensitivity to long wavelengths.

The oven in which the optical bench resides is heated by proportionally-controlled electrical resistance elements. Within the oven, temperatures can vary as much as 5 to 7°C from

point to point, but by much less (e.g., 0.3°C) at the same point over time. The time period during which the resistance elements are on is varied in proportion to the difference between the actual oven temperature and the desired temperature and in proportion to the integral of this difference. To make oven temperature less sensitive to variations in AC line voltage, the time period is also made inversely proportional to the square of the line voltage, as the heat generated by the elements is proportional to the square of the line voltage. The elements are SCR controlled, and are turned on and off only at zero crossings of current.

Figs. 11, 12a, and 12b show the electrical circuits that process the outputs of the photocell 52. Fig. 11 shows the overall circuitry in block diagram form. Panel inputs 118 (e.g., recorder gain) are fed to a central processor 120. The central processor (CPU) initiates the automatic electrical zeroing (nulling) of the photocell outputs, and sends signals via buffers 122 and gain latches 124 to circuitry shown in Fig. 12b to set the gain for display of the chromatogram on a recorder. An analog data acquisition voltage (D.A.V.) is converted to digital and sent by the processor via the input buffers to a panel display 126.

Fig. 12a shows the circuitry for electrical zeroing. The current outputs (AC signals) of the photocells 180, 182 are brought via shielded cable to current-to-voltage converters 130. The AC voltages A, B produced by the converters are summed and amplified by a gain of 2.2 at an amplifier 132, to form the expression $-2.2(A + B)$, which is called SUM. An amplifier 134 subtracts voltage A from voltage B, and adds to the difference the sum of three voltages: SUM, FINE ZERO, and COARSE ZERO. The latter two voltages are produced by multiplying SUM by a negative scale factor. Thus the output of amplifier 134 (ZEROED OUTPUT) can be expressed as

$$[B - A] - 2.2[.33 - .67K_c - .0033K_f][A + B]$$

where K_c is the coarse zero scale factor and K_f is the fine zero scale factor. Scale factors K_c , K_f are set between about zero and about one by the digital circuitry of a block 136, whenever a signal is sent across the AUTOZERO COMMAND lead. Normally zeroing would be done before a chromatogram was generated, but can be done at any time.

The above expression for the ZEROED OUTPUT can be presented in simplified form as

$$[B - A] - K[A + B]$$

where K is the overall scale factor. The expression is independent of variations in the overall brightness of the light beam striking the photocell 52 because the zeroing term ($K[A + B]$) is not a constant, but, like the difference term ($B - A$), is proportional to beam brightness. For example, if the brightness were to rise by 10%, both the difference term and the zeroing term would

similarly rise by 10%, and thus the whole expression would still remain equal to zero. When beam deflection does occur, as the result of refractivity changes, the zeroing term remains roughly constant because of the complementary shape of the two cells 180, 182, which at any horizontal location have roughly the same combined vertical height.

Two successive-approximation registers 138, 140 drive a pair of digital-to-analog converters 142, 144 to form the FINE ZERO and COARSE ZERO signals. Each of converters 142, 144 multiplies the SUM signal by a scale factor set by the digital output of the registers 138, 140. The registers 138, 140 follow a conventional successive approximation algorithm to select the digital outputs or scale factors. About once a second, the registers receive a clock pulse from a chip 148, which produced a slow clock from the much faster processor clock signal. At each clock pulse, the output of a register is adjusted in response to the output of a comparator 146 which indicates whether the applied FINE/COARSE ZERO signal is too large or too small. The input to the comparator 146 is the DC OUTPUT, produced at a filter amplifier 150 (Fig. 12b). A FILTER RESET connection between the zeroing circuitry and the filter amplifier 150 is used during the zeroing process to discharge capacitors in the filter and reset the DC OUTPUT to zero. This allows for a more rapid autozero sequence. The register 138 works first to set the coarse scale factor K_C , and then the register 140 to set the fine scale factor K_F . The AUTOZERO COMMAND is used by the CPU to start the autozero sequence. The AUTOZEROING signal is used to alert the central processor that the refractometer is autozeroing.

Turning to Fig. 12b, there is shown circuitry for processing the ZEROED OUTPUT. An amplifier 152 raises or lowers the signal level in response to command signals 151 from the central processor 120 via the data latch 124. A demodulator 154 (with the help of a phase computing block 153) converts the AC signal to DC, and the filter amplifier 150 smooths the DC signal. A switching block 156 operates during zeroing to turn off the RECORDER and INTEGRATOR signals. It also is used to change the polarity of the DC signal in response to a POLARITY signal from the central processor 120 via the data latch 124. Downstream of the block 156 the DC signal is processed by an amplifier 158, and supplied to an integrator output lead. The DC signal is also processed by an attenuator 160, under control of the central processor via signals 162. The attenuator produces a recorder output 164, which is supplied to a recorder output terminal and to an amplifier 166, and a data acquisition voltage (D.A.V.), which is supplied to the central processor for panel display. A block 168 supplies a mark signal for the recorder in response to the AUTOZERO COMMAND, to indicate on the chromatogram the point at which the sample injection occurs. The CPU issues the AUTOZERO COMMAND at the time of sample injection.

Operation

In operation, the oven surrounding the optical bench and chromatographic column is turned on, and about an hour and one half warm up period is allowed for temperature equalization within the bench. After warm up, solvent is pumped through the sample and reference circuits within the bench. When solvents are changed, sufficient time is allowed for flushing both circuits. Flow is then stopped in the reference circuit (but the reference chamber 72 remains filled with reference liquid). A sample is then injected into the sample column. The electrical output of the refractometer is zeroed by initiating the automatic zeroing sequence described above. Sample passes through the chromatographic column and into the optical bench. Generally speaking, variations in refractivity of the sample cause movement of the light beam with respect to the photocell 52, and thereby change the electrical output, which is plotted against time on a chart recorder, producing a chromatogram.

Temperatures within the chambers 70, 72 of the flow cell are maintained within about 0.0001°C of each other during operation to minimize error. A temperature difference between the two flow cell chambers results in a refractivity difference. Temperature equalization is achieved by providing good thermal insulation around the flow cell, in the form of the air gap 36 between the inner and outer cylinders, the shields 38, and the blackened disk 77; surrounding the flow cell with a thermal mass, in the form of the bridges 56, 58 and the end cap 48; and directing incoming sample flow through a very efficient counterflow heat exchanger to bring the temperature of the sample to the flow cell temperature. Incoming sample upstream of the heat exchanger is typically as much as 1°C (and possibly 2 to 3°C) different in temperature from the flow cell because of spatial differences in oven temperature and because of heat generated by viscous heating inside the inlet tube. This difference in temperature is gradually reduced along the length of the heat exchanger by thermal conduction between the inlet and outlet tubes. At the end of the heat exchanger, whatever very small temperature difference remains is minimized by heat transfer between the end cap 48 and the coil 94 just prior to entry into the flow cell.

The sample heat exchanger is divided into three zones to improve its efficiency, with each successive zone being more thermally stable and closer to the temperature of the flow cell. The construction of the heat exchanger provides good thermal conduction between tubes but very low conduction along the flow direction of the tubes. There is significant heat transfer between the tubes and the surrounding air; thus thermal interaction between the heat exchanger and the region surrounding it must be considered. The first zone, between the outer cylinder 34 and the shield 38, provides a gradual approach in temperature before the heat exchanger enters the optical bench. The length of this zone is greater than 10%

of the length of the sample inlet tube within the bench. Without the first zone, i. e., if the inlet and outlet tubes were joined just outside the entry to the end cap 42, there would be a steeper approach in temperature along the heat exchanger, and much of this approach in temperature would occur along portions of the heat exchanger inside the air gap 36, thereby undesirably transferring heat to or from the bench.

With the preferred arrangement of a first zone outside the bench, the heat exchanger temperature is closer to that of the bench when entering the air gap.

The heat exchanger enters the gap at the photocell end of the bench, thereby assuring that whatever heat transfer to or from the bench does occur is at a location well separated from the flow cell.

This same concept of routing the heat exchanger through increasingly more thermally stable regions is also applied to the second and third zones. In the second zone, the sample heat exchanger is directed along the air gap 36 from the photocell end to the flow cell end, where temperature stability is highest. In the third zone, the sample heat exchanger is coiled behind the flow cell end cap, with each successive coil being closer to the end cap and flow cell.

As a final step, the sample inlet tube alone is coiled in recess 60 of end cap 48 to minimize whatever small temperature difference remains between the incoming sample and the flow cell.

Because the reference solvent does not flow during a measurement, the reference heat exchanger is less sophisticated. It lacks the third coiled zone, and has no copper, heat-conductive braid to surround inlet and outlet tubes. Limited heat exchange is provided on the reference side to maintain rough temperature equalization during flushing of the reference circuit, thereby shortening the period needed to stabilize temperatures after flushing.

The optical elements of the refractometer are shown diagrammatically in Figs. 10a and 10b. For clarity the optical path is shown unfolded, with mirror 78 treated as a window. Fig. 10a shows a horizontal section through the optical path; Fig. 10b shows a vertical section.

Turning to Fig. 10a, a single light ray B is shown to illustrate beam movements. The lens surface 74 on the flow cell 54 focuses the light emerging from the fibre-optic cable outlet 50 onto the photocell 52. The focused image on the photocell is shown diagrammatically in the views on the left side of the Figure. To illustrate the effect caused by rotation of the prism 104, four views (A to D) of the prism in different angular positions are shown along with the corresponding positions of the light beam on the photocell.

Light passing through the chambers 70, 72 is bent in proportion to the difference in the refractive index of the liquids in the two chambers. Referring to Fig. 8, the chambers are conventionally constructed so that the surface 190 in the chamber 70 is parallel to the surface

188 in the chamber 72 and, similarly, so that the surfaces 184 and 186 are parallel. These four surfaces are the four at which light is bent by refraction. If the liquid of the same refractive index is in both chambers, light will be bent by the same amount at each of the corresponding parallel surfaces, and will emerge from the flow cell along a path B which is essentially unaffected by changes in refractivity common to both chambers. If liquid in the two chambers differs in refractive index, light will be bent differentially at these parallel surfaces, and will emerge along a path skewed from the equal-refractivity path. Such a condition is illustrated in Fig. 10a by light ray B'.

The amount by which the light beam is skewed or bent at the flow cell is measured by detecting the position of the image of the beam at the photocell 52. The difference between the electrical outputs of the two triangular cells 180, 182 can very finely resolve the horizontal position of the light beam. Imperfections in alignment of the photocell with the flow cell and other tolerances in the system typically cause these electrical outputs of the two cells to be unequal even when sample and reference liquids have the same refractive index. This initial electrical difference is nulled by the automatic zeroing procedure described above.

Ideally, the light beam location on the photocell 52 should only be a function of the difference in refractive index between sample and reference (and not a function of the location of the bulb filament 101). To achieve this, the light intensity distribution across the fibre-optic outlet 50 must be spatially stable over the time period of chromatographic interest (1 second to several hours). This requires that the light intensity distribution into the fibre optics be stable. As viewed from the fibre-optics inlet 114, the apparent position of the bulb filament 101 varies due to filament distortion and thermal eddies in the air path between the filament and the inlet. Filament movements along the length of the filament (vertical in Fig. 2) are relatively noncritical. Similarly, changes in the filament distance from the fibre-optics inlet are not observable and thus are non-critical. Along the third axis of movement (vertical in Fig. 5) the apparent filament location as viewed by the fibre-optics inlet may be spatially stabilized for the beam location at the photocell to be independent of filament location. To achieve stabilization, a Spatially Homogenizing Optical Modulator (SHOM) in the form of rectangular prism 104 is employed in the light path between the filament and the fibre-optics inlet. The prism provides an optical path offset which is a function of its rotation position. When the prism rotates, the filament optically appears to sweep across the face of the fibre-optics inlet 114. In position A, the prism is so oriented that the light from the filament 101 is bent outside the acceptance angle of the fibres in the cable 18, and negligible light is transmitted to the bench. In position B, the prism has rotated sufficiently for light to be transmitted through at least some of the fibres in the cable. In

position C, the prism has swept the filament image across the face of the fibre-optics inlet. In position D, the prism has moved the image to a position beyond the acceptance angle of the fibres, and again negligible light is transmitted. As the prism rotates further, the beam first reappears beyond the acceptance angle of the fibres, as in position A, and then another sweep begins. The sweeping action, including the period of negligible light transmission, occurs two times during each revolution of the prism, or about 100 times per second.

If the filament 101 moves or appears to move, this has the effect of changing the time at which the beam starts and finishes its sweep across the fibre-optics inlet. That is, only the phase of the beam movement is altered by movement of the filament. The electronics described above compute the average or middle position swept by the image. The electronics are insensitive to such phase or time shifts, and thus the undesirable effects of filament shift are minimized.

The apparent light source position is further stabilized by using the randomized fibre-optics bundle 18. In a perfectly randomized fibre-optics bundle, adjacent fibres at one end of the bundle are randomly distributed at the other end. Therefore, increasing the light on one side of the bundle input while decreasing it on the other side results in no change in the light distribution across the fibre-optics output end. In actual practice, the randomization in a bundle is not perfect, and some change does occur at the output end. But using the randomized fibre-optics does further decrease the effect of filament motion on beam movement at photocell 52.

As can be seen in Fig. 10b, the optics do not focus the beam onto the photocell in the vertical direction, as done in the horizontal direction. Instead, light emerging from outlet 50 of cable 18 remains unfocused in vertical planes, thereby producing for each point of light at the outlet a vertical line of light at the photocell. The vertical height of this line is limited by the vertical height of mirror 78, which acts as a mask. Light rays from individual points, e.g., points X and Y, on the cable outlet 50 fan out, but only rays inside of limit rays X_1 , X_2 (Y_1 , Y_2 for point Y) reach the photocell. (Other rays are not reflected through the photocell.) The vertical heights of the mirror 78, photocell 52, and cable outlet 50 and the spacing between the flow cell and photocell ends of the bench are all selected so that the limit rays for all points on the cable outlet strike fully above and fully below the triangular cells 180, 182 of the photocell. Limit rays for point X and point Y, at the top and bottom extremities of the cable outlet, are shown in Fig. 10b. Thus each point on the cable outlet produces a line of uniform intensity at the photocell. And these lines all overlap over the photocell, thereby assuring a uniform vertical intensity across the photocell no matter what vertical variation in intensity may exist at the cable outlet (e.g., due to variation in filament intensity in the vertical direction). The end result is the light

intensity profile shown at the left side of Fig. 10b. Across the vertical height of the photocells the intensity is uniform; outside the photocells the intensity falls off to zero. Vertical uniformity of light intensity at the photocells is needed to linearly determine the horizontal light beam location on the triangular-shaped cells 180, 182. (A vertical variation in intensity would be indistinguishable from a horizontal movement of the light beam.)

Other embodiments are within the following claims. For example, reflective coatings other than gold could be used (e.g., aluminium, silver, or a multilayer coating); an anti-reflection coating could be substituted for black epoxy coating 76, with a light trap positioned behind and external to the cell to absorb light passing through the coating; quartz glass and the like could replace the borosilicate glass used for the flow cell; and the glass pieces of the flow cell could be joined together by diffusion bonding or with adhesive.

CLAIMS

1. Apparatus for measuring changes in the refractivity of a fluid flowing through a temperature-controlled cell, wherein an inlet tube for carrying sample fluid to said cell and an outlet tube for carrying sample fluid from said cell are mounted in a heat-exchanging relationship with each other.
2. Apparatus as claimed in claim 1, wherein said tubes extend side-by-side in a counterflow relationship to cause the temperatures of fluid flowing through said inlet tube increasingly to approach the temperature of said cell through at least a first heat-exchange zone.
3. Apparatus as claimed in claim 1 or claim 2, wherein said cell is mounted inside a housing and said first zone is inside said housing.
4. Apparatus as claimed in claim 3, wherein said tubes extend through at least a second heat-exchange zone upstream of said first zone, said second zone being inside said housing.
5. The improvement of claim 4, wherein said tubes extend through a third heat-exchange zone outside said housing.
6. Apparatus as claimed in any one of the preceding claims, wherein at least one of said tubes is coiled.
7. Apparatus as claimed in any one of claims 1 to 6 and including a light source to direct a light beam through a measurement zone of said cell to a detector, in order that movement of said beam in a measurement direction with respect to said detector may give an indication of the measurement made in said zone and comprising means for modulating, through a preselected amplitude in a modulation direction, the position of said beam with respect to said measurement zone, said amplitude being independent of light beam movements at said light source or in the path of said beam between said source and said modulating means, whereby said measurement can be made substantially independent of said beam movements in said modulation direction.

8. Apparatus as claimed in claim 7, wherein said modulation direction is said measurement direction.

9. Apparatus as claimed in claim 7 and 8, further comprising second means for modulating the position of said beam in a second modulation direction with respect to said beam, whereby said measurement can be made substantially independent of said beam movements in said first-mentioned and second modulation direction.

10. Apparatus as claimed in claim 7, 8 or 9, wherein said first modulating means cyclically sweeps said beam between a first and a second position along said first modulation direction.

11. Apparatus as claimed in claim 10, wherein said first modulating means includes means for substantially extinguishing said beam momentarily at said first and second positions.

12. Apparatus as claimed in any one of claims 7 to 11, wherein said modulating means is located along the path of said light beam ahead of said zone.

13. Apparatus as claimed in claim 12, wherein said modulating means comprises optical modulating means for modulating said beam.

14. Apparatus as claimed in any one of claims 1 to 6 and of the type including a light source directing a light beam through a measurement zone to a detector, wherein movement of said beam in a measurement direction with respect to said detector gives an indication of the measurement made in said zone, or as claimed in any one of claims 7 to 13, comprising means for permitting said light beam to pass unfocused in selected planes from said light source through said measurement zone to said detector.

15. Apparatus as claimed in claim 14, wherein said means comprises lens means for focusing said light beam generally only in said measurement direction, and masking means for blocking portions of said light beam so that light from individual points on said source is spread at the detector into lines of light that substantially overlap at the detector, whereby variation in the intensity of said light source along the unfocused direction does not substantially affect the measurement at said detector.

16. Apparatus as claimed in any one of the preceding claims, wherein said cell comprises an integral reflective layer for reflecting a or said light beam back through said cell.

17. Apparatus as claimed in claim 16, wherein said reflective layer comprises a reflective coating applied to an exterior surface of said cell.

18. Apparatus as claimed in claim 17, wherein said reflective coating covers a limited area of said surface and thereby reflects only a portion of said light beam passing through said cell, whereby said reflective coating functions as a mask to block portions of said beam.

19. Apparatus as claimed in claim 17 or 18, wherein said area covered by said reflective coating is selected so that no more than fifty percent of the reflected portion of said beam is light that does not pass through said sample

within said cell.

20. Apparatus as claimed in any one of the preceding claims, being apparatus for measuring deflection of a light beam by sensing said beam with means providing two optical measurements, and providing an electrical output dependent upon the difference between said two measurements, comprising electrical circuitry for including in said output an offset term dependent upon the magnitude of at least one of said measurements, and means for zeroing said apparatus by adjusting said offset term to make said output equal to a predetermined base value.

21. Apparatus as claimed in claim 20, wherein said offset term is dependent upon both said measurements.

22. Apparatus as claimed in claim 21, wherein said output is dependent upon the difference between quantities A and B, which are in turn respective measures of said two measurements, said apparatus being of the type in which the sum $A + B$ is substantially insensitive to changes in said measurements, and said offset sum is dependent on said sum so as to maintain zeroing accuracy as said measurements change.

23. Apparatus as claimed in claim 22, wherein said offset term is the product of said sum and a constant determined by said means for zeroing.

24. Apparatus as claimed in any one of the preceding claims, wherein said cell comprises an integral curved surface for acting as a lens to focus a or said light beam.

25. Apparatus as claimed in claim 24, wherein said curved surface is the first surface through which said beam passes.

26. Apparatus as claimed in claim 25, wherein said surface has curvature in a first family of parallel planes but no curvature in a second family of parallel planes orthogonal to said first planes.

27. Apparatus as claimed in any one of the preceding claims, wherein said cell includes an opaque masking portion for absorbing portions of a or said light beam.

28. Apparatus as claimed in any one of the preceding claims, including circuitry of the type including analog circuit means for producing an analog output in response to an input and digital circuit means for sampling said output, said analog circuit means including a charge storage element that can become charged in response to said input, further comprising charge dissipation means for dissipating the charge built up in said charge storage element during an interval prior to sampling of said output by said digital circuit means.

29. Apparatus as claimed in claim 28, wherein said digital circuit means and analog circuit means are connected in a loop and said digital means includes means for providing said input to said analog circuit and for periodically changing said input in response to changes in said sampled output.

30. Apparatus as claimed in claim 29, wherein said digital circuit means includes means for changing said input so that said output

approaches a desired value.

31. Apparatus as claimed in claim 30, wherein said desired value is zero.

32. Apparatus for effecting a measurement on

5 a fluid substantially as hereinbefore described with reference to, and as shown in, the accompanying drawings.

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